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EXAMINER	
STEADMAN, DAVID J	

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1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,539	ABE ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *3,4 and 7-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,6,34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Appendix A sequence alignment*.

DETAILED ACTION

Status of the Application

[1] Claims 1-35 are pending in the application.

[2] Applicant's amendment to the claims, filed on 2/24/10, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims.

[3] Applicant's amendment to the abstract and specification, filed on 2/24/10, is acknowledged.

[4] Receipt of a marked-up copy of the substitute specification filed on 7/28/06, is acknowledged.

[5] Receipt of a certified English-language translation of Japanese patent application number 2004-019251, filed on 2/24/10, is acknowledged.

[6] Applicant's remarks filed on 2/24/10 in response to the non-final Office action mailed on 11/24/09, have been fully considered and are deemed to be persuasive to overcome at least one of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

[7] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Election/Restriction

[8] Claims 3-4 and 7-33 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable

generic or linking claim. Election was made without traverse in the reply filed on 3/11/09.

[9] Claims 1-2, 5-6, and 34-35 are being examined on the merits.

Specification/Informalities

[10] The objection to the title of the invention as being non-descriptive is withdrawn in view of the instant specification amendment to replace the title with ---Neoculin Acidic Subunit, A Taste-Modifying Polypeptide---.

[11] The objection to the abstract of the disclosure is withdrawn in view of the instant amendment to the abstract.

[12] The objection to the substitute specification filed on 7/28/06 because there is no marked-up version as required by 37 CFR 1.125(c) is withdrawn in view of the instant filing of a marked-up copy of the substitute specification filed on 7/28/06.

Claim Objection

[13] The objection to claims 1-2 and 5-6 in the recitation of the abbreviations "NAS", "NBS", and "PNAS" is withdrawn in view of the instant claim amendment.

[14] The objection to claims 1 and 5 as reciting the improper sequence identifier "SEQ ID NO.2", "SEQ ID NO.6", and "SEQ ID NO.3", is withdrawn in view of the instant claim amendment to recite "SEQ ID NO:2", "SEQ ID NO:6", and "SEQ ID NO:3", respectively.

[15] The objection to claim 5 in the recitation of "which polypeptide grows to the mature polypeptide NAS via processing" is withdrawn in view of the instant claim amendment.

Claim Rejections - 35 USC § 112, Second Paragraph

[16] The rejection of claims 1-2 and 5-6 as lacking antecedent basis in the recitation of "the neoculin dimer" is withdrawn in view of the instant claim amendment to delete the phrase at issue.

[17] The rejection of claims 1-2 and 5-6 as being indefinite in the recitation of "which polypeptide" is withdrawn in view of the instant claim amendment to delete the phrase at issue.

[18] The rejection of claims 5-6 as being indefinite in the recitation of "grows to the mature polypeptide NAS via processing" is withdrawn in view of the instant claim amendment to delete the phrase at issue.

[19] Claims 1-2 and 5-6 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by the instant claim amendment.

Claims 1 (claim 2 dependent therefrom) and 5 (claim 6 dependent therefrom) recite the limitation "the amino acid sequence with the substitution...of one to five amino acids". The use of the article "the" indicates there is a single amino acid sequence to

which the noted phrase references. However, the phrase encompasses a plurality of sequences and it is unclear as to which of the sequences is intended as being *the* amino acid sequence. It is suggested that applicant clarify the meaning of the noted phrase by, *e.g.,* amending part (B) of claim 1 to recite, "a polypeptide comprising the amino acid sequence of SEQ ID NO:2, except for substitution, deletion, insertion, addition, or inversion of no more than one to five amino acids in the amino acid sequence of SEQ ID NO:2 in the sequence listing".

Claim Rejections - 35 USC § 101

[20] The rejection of claims 1-2 and 5-6 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in view of the instant amendment to claims 1-2 and 5-6 to recite "An isolated…"

Claim Rejections - 35 USC § 112, First Paragraph

[21] The written description rejection of claims 1-2 and 5-6 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons set forth below. The rejection as it applied to previous claims 1-2 and 5-6 was fully explained in a prior Office action. See [14] beginning at p. 5 of the Office action mailed on 11/24/09.

Claim 1 (claim 2 dependent therefrom) is drawn to (in relevant part) a genus of neoculin acidic subunit (NAS) polypeptides comprising the amino acid sequence with the substitution, deletion, insertion, addition or inversion of one to five amino acids in the amino acid sequence of SEQ ID NO:2.

Claim 5 (claim 6 dependent therefrom) is drawn to (in relevant part) a genus of neoculin acidic subunit precursor (PNAS) polypeptides comprising the amino acid sequence with the substitution, deletion, insertion, addition or inversion of one to five amino acids in the amino acid sequence of SEQ ID NO:3.

The term "with" in the phrase "with the substitution…" is broadly and reasonably interpreted as being synonymous with "comprising", which is inclusive and open-ended. Thus, the phrase "the amino acid sequence with the substitution, deletion, insertion, addition or inversion of one to five amino acids" is interpreted as encompassing *at least* one to five amino acid variations relative to SEQ ID NO:2 or 3, but the number of variations being unlimited. Put another way, the amino acid sequences of the genus of polypeptides of parts (B) of claims 1 and 5 is unlimited. Also, the function of the genus of polypeptides is unlimited.

MPEP 2163.II.A.2.(a).i) states, "Whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather is a factual determination reached by considering a number of factors. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention". For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings,

or by disclosure of relevant, identifying characteristics, *i.e.,* structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 further states that a "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In this case, the specification discloses an actual reduction to practice of a single representative species of the genus of NAS and PNAS proteins as encompassed by the claims, *i.e.,* SEQ ID NO:2 and 3, respectively. Other than these species, the specification fails to disclose any other species of the genus of recited NAS or PNAS polypeptides as encompassed by the claims by complete or partial structure, drawings, or chemical formula. Also, there is no art-recognized correlation between the function of SEQ ID NO:2 or 3 and its corresponding amino acid sequence. It is well known that the amino acid sequence and resulting conformation of a polypeptide determines its function. The level of knowledge and skill in the art does not allow those skilled in the art to structurally envisage or recognize those structures of variants of SEQ ID NO:2 or 3, particularly as the genus is unlimited with respect to amino acid sequence and function. No common structural attributes identify the members of the substitution, deletion and insertion variant genus. Because the disclosure fails to describe the common attributes or characteristics that identify substitution, deletion and insertion variant members of the

genus, and because the genus is highly variant with respect to both structure, *i.e.*, amino acid sequence, and function, the two disclosed representative species are insufficient to describe the genus, even when considered in light of the general knowledge in the art concerning amino acid modification(s).

One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus, and thus, that the applicant was not in possession of the recited genus. The claimed subject matter is not supported by an adequate written description because a representative number of species has not been described.

RESPONSE TO ARGUMENT: Beginning at p. 23 of the instant remarks, applicant argues the written description rejection is obviated by amendment to claims 1 and 5. However, this is not found persuasive because, as noted above, the genus of polypeptides of parts (B) of claims 1 and 5 is both structurally and functionally unlimited and the two disclosed representative species of polypeptides fail to reflect the substantial variation among the members of the claimed genus. As such, the specification fails to describe all polypeptides encompassed by the claimed genus.

[22] The scope of enablement rejection of claims 1-2 and 5-6 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons set forth below. The rejection as it applied to previous claims 1-2 and 5-6 was fully explained in a prior Office action. See [15] beginning at p. 9 of the Office action mailed on 11/24/09.

Claims 1-2 and 5-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide comprising SEQ ID NO:2 or 3, optionally glycosylated with an N-linked sugar chain comprising mannose/N-acetylglucosamine/fucose/xylose at a ratio of 3/2/1/1 when the polypeptide is purified from the fruit of *Curculigo latifolia* plant, does not reasonably provide enablement for all polypeptides as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

"The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue." *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

The nature of the invention: According to the specification, the nature of the invention is a heterodimeric protein from the *Curculigo latifolia* plant comprising two subunits, a neoculin acidic subunit (NAS) having the amino acid sequence of SEQ ID

NO:2 and a neoculin basic subunit (NBS) having the amino acid sequence of SEQ ID NO:6, where the heterodimer has a taste-modifying function (p. 2, first full paragraph; p. 4, first and second paragraphs).

The breadth of the claims: As noted above, claim 1 (claim 2 dependent therefrom) is drawn to (in relevant part) a neoculin acidic subunit (NAS) polypeptide comprising the amino acid sequence with the substitution, deletion, insertion, addition or inversion of one to five amino acids in the amino acid sequence of SEQ ID NO:2.

Claim 5 (claim 6 dependent therefrom) is drawn to (in relevant part) a neoculin acidic subunit precursor (PNAS) polypeptide comprising the amino acid sequence with the substitution, deletion, insertion, addition or inversion of one to five amino acids in the amino acid sequence of SEQ ID NO:3.

The term "with" in the phrase "with the substitution…" is broadly and reasonably interpreted as being synonymous with "comprising", which is inclusive and open-ended. Thus, the phrase "the amino acid sequence with the substitution, deletion, insertion, addition or inversion of one to five amino acids" is interpreted as encompassing *at least* one to five amino acid variations relative to SEQ ID NO:2 or 3, but the number of variations being unlimited. Put another way, the amino acid sequences of the scope of polypeptides of parts (B) of claims 1 and 5 is unlimited. Also, the function of the scope of polypeptides is unlimited.

The amount of direction provided by the inventor; The existence of working examples: The specification discloses a single working example of an NAS polypeptide and a single working example of a PNAS polypeptide as encompassed by the claims,

i.e., SEQ ID NO:2 and SEQ ID NO:3, respectively. However, these working examples, in combination with the remaining disclosure of the specification fail to provide the necessary guidance for making the entire scope of claimed polypeptides as noted above. Also, the specification fails to provide guidance for using those polypeptides that do not maintain the activity of forming a heterodimer with SEQ ID NO:6 and do not maintain a sweet taste.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: The amino acid sequence of a polypeptide determines the polypeptide's structural and functional properties. Predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity/utility requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (*i.e.*, expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within a protein's sequence where modifications can be made with a reasonable expectation of success in obtaining a polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, *e.g.,* multiple substitutions.

It is well-known in the art that even a single amino acid alteration can alter the function of a polypeptide. See, *e.g.,* MPEP 2144.08.II.A.4.(c), which states, "[i]n the area of biotechnology, an exemplified species may differ from a claimed species by

a conservative substitution ("the replacement in a protein of one amino acid by another, chemically similar, amino acid... [which] is generally expected to lead to either no change or only a small change in the properties of the protein." Dictionary of Biochemistry and Molecular Biology 97 (John Wiley & Sons, 2d ed. 1989)). The effect of a conservative substitution on protein function depends on the nature of the substitution and its location in the chain. Although at some locations a conservative substitution may be benign, in some proteins only one amino acid is allowed at a given position. For example, the gain or loss of even one methyl group can destabilize the structure if close packing is required in the interior of domains. James Darnell et al., Molecular Cell Biology 51 (2d ed. 1990)."

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of isolating or generating variants of a polypeptide were known in the art at the time of the invention, it was not routine in the art to screen for any and all polypeptide variants as encompassed by the claims.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required to make and use all polypeptides as broadly encompassed by the claims, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable

correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

[23] The rejection of claims 1-2 and 5-6 under 35 U.S.C. 102(a) as being anticipated by Suzuki et al. ("Recombinant curculin heterodimer exhibits, taste-modifying and sweet-tasting activities", *FEBS Lett.* 573:135-138, 2004; cited in the IDS filed on 7/28/06; hereafter "Suzuki") OR Shirasuka et al. ("Neoculin as a New Taste-modifying Protein Occurring in the Fruit of *Curculigo latifolia*", *Biosci. Biotechnol. Biochem.* 68:1403-1407, 2004; cited in the IDS filed on 7/28/06; hereafter " Shirasuka") is withdrawn in view of the instant filing of a certified English-language translation of Japanese patent application number 2004-019251, which perfects applicant's claim to priority under 35 U.S.C. 119(a)-(d). The disclosure of the English-language translation of Japanese patent application number 2004-019251 appears to provide adequate descriptive support for the claimed invention at pp. 4-6, 12, and 14-17.

[24] Claim(s) 1 and 5 are newly rejected under 35 U.S.C. 102(b) as anticipated by Yamashita et al. (Purification and Complete Amino Acid Sequence of a New Type of Sweet Protein with Taste-modifying Activity, Curculin", *J. Biol. Chem.* 265:15770-15775,

1990; hereafter "Yamashita"; cited in the IDS filed on 7/28/06). This rejection is necessitated by the instant claim amendment.

As noted above, the term "with" in the phrase "with the substitution..." in parts (B) of claims 1 and 5 is broadly and reasonably interpreted as being synonymous with "comprising", which is inclusive and open-ended. Thus, the phrase "the amino acid sequence with the substitution, deletion, insertion, addition or inversion of one to five amino acids" is interpreted as encompassing *at least* one to five amino acid variations relative to SEQ ID NO:2 or 3, but the number of variations being unlimited. Put another way, the amino acid sequence of the polypeptide of parts (B) of claims 1 and 5 is unlimited. Also, the function of the polypeptide of parts (B) of claims 1 and 5 is unlimited.

The reference of Yamashita teaches isolation of a polypeptide referred to as curculin (p. 15770, column 2). This anticipates claims 1 and 5 as written.

Claim Rejections - 35 USC § 102/103

[25] The rejection of claims 1 and 5 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Yamashita (*supra*) as evidenced by Suzuki (*supra*) and Shimizu-Ibuka et al. (*J. Mol. Biol.* 359:148-158, 2006; hereafter referred to as "Shimizu-Ibuka") is withdrawn. The rejection is withdrawn solely in favor of the new rejection of claims 1 and 5 under 35 U.S.C. 102(b) set forth above because parts (B) of claims 1 and 5 have been amended to encompass a polypeptide with unlimited amino acid sequence and function.

[26] The rejection of claims 2 and 6 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Yamashita (*supra*) as evidenced by Suzuki (*supra*) and Shimizu-Ibuka et al. (*J. Mol. Biol.* 359:148-158, 2006; hereafter referred to as "Shimizu-Ibuka") is maintained for the reasons of record and the reasons set forth below. The rejection as it applied to previous claims 1-2 and 5-6 was fully explained in a prior Office action. See [17] beginning at p. 16 of the Office action mailed on 11/24/09. Claims 34-35 are included in the instant rejection for reasons set forth below. Thus, claims 2, 6, and 34-35 are rejected herein.

The reference of Yamashita teaches an extract of *Curculigo latifolia* fruit that is sweet and comprises curculin (p. 15570, column 1) and teaches isolation of curculin (p. 15770, column 2).

The evidentiary references of Suzuki and Shimizu-Ibuka are relied upon as extrinsic evidence that makes clear that the missing descriptive matter is necessarily present in the thing described in the reference, *i.e.,* SEQ ID NO:6 is present in the extract of *Curculigo latifolia* fruit; SEQ ID NO:2 is a subunit of the curculin polypeptide of Yamashita; and that the NAS of curculin is glycosylated, and that it would be so recognized by persons of ordinary skill. Put another way, the evidentiary references of Suzuki and Shimizu-Ibuka are relied upon to show that the extract of *Curculigo latifolia* fruit as taught by Yamashita comprises the PNAS of SEQ ID NO:6; to show that the curculin polypeptide of Yamashita is composed of two subunits, one of the subunits

being the NAS of SEQ ID NO:2; and that the NAS of the polypeptide of Yamashita is glycosylated according to claims 2 and 6.

Evidentiary reference Suzuki discloses that the only active form of curculin from the fruit of *Curculigo latifolia* is a heterodimer of curculin1 and curculin2 (which correspond to NBS of SEQ ID NO:6 and NAS of SEQ ID NO:2, respectively, as shown in Figure 1 at p. 136 of Suzuki), where *only* the curculin1-2 heterodimer exhibits sweet-tasting and taste-modifying activities, whereas the respective homodimers do not (p. 136, column 2). The amino acid sequence of curculin2 is 100% identical to SEQ ID NO:2 herein (See Appendix B sequence alignment at pp. 20-21 of the Office action mailed on 11/24/09).

Similarly, evidentiary reference Shimizu-Ibuka teaches "Curculin, occurring in the fruit of *Curculigo latifolia*…was initially regarded as a homodimer consisting of two identical subunits, although the recombinant homodimer was devoid of any taste-modifying activity. A recent study revealed that the active component is actually a heterodimeric protein, which was designated as 'neoculin'. This protein consists of an acidic, glycosylated subunit (neoculin acidic subunit, NAS) of 113 amino acid residues…"

Regarding claims 2 and 6, according to the specification, the polypeptide isolated from the fruit of *C. latifolia* is glycosylated with an N-linked sugar chain comprising mannose/N-acetylglucosamine/fucose/xylose at a ratio of 3/2/1/1 (p. 41) and thus because curculin of Yamashita is isolated from the fruit of *C. latifolia,* it is necessarily

glycosylated with an N-linked sugar chain comprising mannose/N-acetylglucosamine/fucose/xylose at a ratio of 3/2/1/1.

This anticipates claims 2, 6, and 34-35 as written.

RESPONSE TO ARGUMENT: Beginning at p. 25 of the instant remarks, applicant argues the references of Suzuki and Shimizu-Ibuka are not available as prior art under 35 U.S.C. 102 because their publication dates are after the foreign priority date.

Applicant's argument is not found persuasive. According to MPEP 2124, post-filing publications can be properly applied to show "characteristics and properties of a material". Here, the references of Suzuki and Shimizu-Ibuka are not relied upon as prior art under 35 U.S.C. 102. Rather, as noted in the prior Office action, the references of Suzuki and Shimizu-Ibuka are relied upon as evidentiary references in accordance with MPEP 2131.01, showing that a characteristic not disclosed in the Yamashita reference is inherent, *i.e.,* the isolated curculin polypeptide of Yamashita is a heterodimer of two subunits, where one of the subunits of curculin comprises the amino acid sequence of SEQ ID NO:2. The examiner has applied the references of Suzuki and Shimizu-Ibuka as extrinsic evidence that makes clear that the missing descriptive matter, *i.e.,* SEQ ID NO:2, is necessarily present in the thing described in the reference, *i.e.,* the curculin polypeptide of Yamashita, and that it would be so recognized by persons of ordinary skill.

Applicant further argues Yamashita discloses *curculin,* not the claimed *neoculin subunit* polypeptide, where the claimed polypeptide has a stronger taste modifying activity relative to curculin. Applicant argues the polypeptide of Yamashita has an amino acid sequence that has 29 amino acid differences relative to the amino acid sequence of SEQ ID NO:2, and thus is excluded from the claims.

Applicant's argument is not found persuasive. Initially it is noted that the amino acid sequences and functions of the polypeptides of claims 1 and 5 are unlimited and applicant's argument addressing at least these claims is moot.

To the extent claims 1-2, 5-6, and 34-35 are limited to the amino acid sequences of SEQ ID NO:2 or 3, the examiner acknowledges that the amino acid sequence disclosed by Yamashita at p. 15772 is distinct from that of SEQ ID NO:2 and 3. However, the amino acid sequence disclosed by Yamashita at p. 15772 is not relied upon as anticipating the claimed invention. As shown in the sequence alignment of Appendix A, the amino acid sequence disclosed by Yamashita is the NBS subunit of SEQ ID NO:6 of curculin. Although Yamashita does not expressly disclose the NAS subunit of SEQ ID NO:2 of curculin, evidentiary references Suzuki and Shimizu-Ibuka provide evidence that the NAS subunit of SEQ ID NO:2 of curculin was *necessarily* present in the curculin of Yamashita. MPEP 2112.I makes clear that "the discovery of a previously unappreciated property of a prior art composition…does not render the old composition patentably new to the discoverer". See also MPEP 2112.II, "[t]here is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in

the prior art reference". In accordance with MPEP 2112.IV, the examiner has provided a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art".

Applicant attempts to distinguish the curculin of Yamashita from neoculin by reference to a comparison of the respective taste-modifying activity (Example 10 at pp. 47-49). However, the "curculin" used in the comparison is actually a *homodimer* of a single subunit of curculin (see p. 48, middle), where evidentiary references Suzuki and Shimizu-Ibuka clearly teach curculin is a *heterodimer*. As such, the "curculin" used in the taste comparison is not the curculin of Yamashita. Rather, the neoculin heterodimer appears to be the same as the curculin of Yamashita.

At least for these reasons, the claimed invention is anticipated by the reference of Yamashita.

Conclusion

[27] Status of the claims:

Claims 1-35 are pending.

Claims 3-4 and 7-33 are withdrawn from consideration.

Claims 1-2, 5-6, and 34-35 are rejected.

No claim is in condition for allowance.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath Rao can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/David J. Steadman/
Primary Examiner, Art Unit 1656

APPENDIX A – Sequence alignment, Yamashita polypeptide and SEQ ID NO:6

Query sequence 1

```
>YAMASHITA POLYPEPTIDE
MAAKFLLTILVTFAAVASLGMADNVLLSGQTLHADHSLQAGAYTLTIQNKCNLVKYQNGR
QIWASNTDRRGSGCRLTLLSDGNLVIYDHNNNDVWGSACWGDNGKYALVLQKDGRFVIYG
PVLWSLGPNGCRRVNGGITVAKDSTEPQHEDIKMVINN
```

Query sequence 2

```
>SEQ ID NO:6
DNVLLSGQTLHADHSLQAGAYTLTIQNKCNLVKYQNGRQIWASNTDRRGSGCRLTLLSDG
NLVIYDHNNNDVWGSACWGDNGKYALVLQKDGRFVIYGPVLWSLGPNGCRRVNG
```

Full-length alignment between two sequences

```
>>SEQ ID NO:6                                              (114 aa)
 s-w opt: 805  Z-score: 1000.9  bits: 190.9 E(): 6.1e-54
Smith-Waterman score: 805;  100.000% identity (100.000% ungapped) in 114 aa overlap (23-136:1-
114)

               10        20        30        40        50        60
YAMASH MAAKFLLTILVTFAAVASLGMADNVLLSGQTLHADHSLQAGAYTLTIQNKCNLVKYQNGR
                           ::::::::::::::::::::::::::::::::::::::
SEQ                        DNVLLSGQTLHADHSLQAGAYTLTIQNKCNLVKYQNGR
                                   10        20        30

               70        80        90       100       110       120
YAMASH QIWASNTDRRGSGCRLTLLSDGNLVIYDHNNNDVWGSACWGDNGKYALVLQKDGRFVIYG
       ::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::::
SEQ    QIWASNTDRRGSGCRLTLLSDGNLVIYDHNNNDVWGSACWGDNGKYALVLQKDGRFVIYG
       40        50        60        70        80        90

              130       140       150
YAMASH PVLWSLGPNGCRRVNGGITVAKDSTEPQHEDIKMVINN
       ::::::::::::::::
SEQ    PVLWSLGPNGCRRVNG
     100       110
```